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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/564,429	04/24/2006	Michael Buschle	SONN:084US/10512512	7323

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EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	**PAPER NUMBER**
1648	
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08/28/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/564,429	BUSCHLE ET AL.	
	Examiner	Art Unit	
	ZACHARIAH LUCAS	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *, 39, 40, 42, 45, 48, 54, 58-60, 63, 67-69, 71-73, 75, and 76* is/are pending in the application.

4a) Of the above claim(s) *42,45,54,58,59,63,67-69,71,75 and 76* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34,39,40,48,60,72 and 73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 34, 39, 40, 42, 45, 48, 54, 58-60, 63, 67-69, 71-73, 75, and 76 are pending in the application.

2. In the prior action, mailed on November 6, 2007, claims 34, 35, 39, 40, 42, 45, 48, 54, 58-69, 71-73, 75, and 76 were pending in the application; with claims 42, 45, 54, 58, 59, 63, 66-69, 71, 75, and 76 withdrawn from consideration, and claims 34, 35, 39, 40, 48, 60-62, 64, 65, 72, and 73 are under consideration and rejected.

3. In the Response of July 7, 2008, the Applicant amended claims 34, 39, 40, 42, 45, 48, 54, 67, and 68; and cancelled claims 35, 61, 62, 64-66.

4. Claims 34, 39, 40, 48, 60, 72, and 73 are under consideration.

Specification

5. **(Prior Objection- Withdrawn)** The disclosure was objected to because of minor informalities. In view of the amendments to the specification, the objection is withdrawn.

Sequence Listing

6. **(Prior Objection- Withdrawn)** The specification was objected to for referring to sequences (the deoxy-Inosine/deoxy-Cytosine ODN on page 38) without also properly identifying them by the sequence identifier assigned to them in the sequence listing as required by 37 CFR 1.821(d). In view of the resubmitted sequence listing, the objection is withdrawn.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. **(Prior Rejection- Maintained)** Claims 34, 35, 39, 40, 48, 60-62, 64, 65, 72, and 73 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The rejection is withdrawn from cancelled claims 35, 61, 62, 64, and 65. The rejection is maintained against pending claims 34, 35, 39, 40, 60, 72, and 73.

The Applicant traverses the rejection on three grounds.

The first argument is that human clinical evidence has been provided in the application, and supplemented in the Klade declaration submitted with the Response. This argument is not found persuasive. As was indicated in the prior action, the rejected claims are drawn to an HCB vaccine. By identifying the claimed compositions as a vaccine, the claim is implicitly providing a requirement for a therapeutic benefit upon administration of the composition.

As was indicated in the prior action, the human experimental data provided in the application, and now in the Klade declaration, provides evidence only that the claimed compositions are effective at inducing immunogenic responses, and that they appear to be safe and tolerated in individuals to whom they are administered. However, as was described in the prior action, the teachings in the art indicate that such showings are sufficient to demonstrate efficacy as a vaccine against HCV. In particular, it was noted that the art indicated that vaccines against HCV had been sought but had not been achieved by those in the art despite prior success in the induction of similar immune responses to those achieved in the experimental data of present application using similar peptides to those present in the claimed compositions. In view

of such teachings, the mere demonstration that the claimed composition was successful in the induction of such immune responses is not found sufficient to demonstrate efficacy as an anti-HCV vaccine. I.e., evidence that such responses were achieved does not demonstrate that the composition would provide a therapeutic benefit against the viral infection.

Applicant's second argument is a two part argument that a demonstration of therapeutic efficacy in human clinical trials is not a requirement for patentability, and that it is the Examiner's burden to give reasons for a conclusion of lack of correlation between in vitro and in vivo assays as evidence of enablement. The latter portion of the argument is not found persuasive for the reasons indicated above, and in the prior action. I.e., the teachings in the art indicate that the mere ability to induce an anti-HCV immune response does not demonstrate that the composition would be an effective therapeutic in view of the uncertainty and complexity in the art of developing anti-HCV vaccines, and the uncertainty in the art as to what the correlates of protection against HCV are. In view of the teachings cited in the prior action relating to such uncertainty, complexity, and limited understanding in the art of developing HCV vaccines, there is adequate grounds to reject the claims as lacking enabling support for an HCV vaccine where the only data presented is that demonstrating only the ability to induce and immune response.

With respect to the argument that there is not requirement for human trials for the patentability of pharmaceutical claims, it is noted that this is a general rule, and that the rule applies to making a determination as to the utility of claimed invention under 35 USC § 101. See, MPEP 2105 § IV. The Examiner is willing to concede that such a general rule would also apply in making enablement determinations. However, even in the presence of the general rule, it

is noted that the MPEP also indicates that "[c]laims directed to a method of treating or curing a disease for which there have been no previously successful treatments or cures warrant careful review for compliance" with the patentability statutes (MPEP 2105 § VI). I.e., even with respect to utility, which has a lower requirement of operability than does enablement, the MPEP directs that careful consideration and more than the usual showing may be required with respect to specific diseases, such as those that have been resistant to therapy.

As was indicated by the art in the prior action, HCV is such a disease requiring additional consideration and evidence. Moreover, the MPEP specifically states that once the examiner has established a reasonable basis to question the enablement of the claimed invention, as has been done in the present application, the burden falls on the Applicant to provide evidence that would be convincing to one skilled in the art. MPEP 2164.05. In the presence case, the teachings in the prior art indicate that more data regarding the efficacy of the claimed composition as an effective vaccine is required than the mere demonstration of safety and the ability to induce an immune response. In the present case, evidence that the claimed composition would be capable of providing a therapeutic response is required.

The next argument is an assertion that the teachings of the Wedemeyer declaration demonstrate that the Applicant is enabled for the claimed composition. It is agreed that the declaration is sufficient evidence for the enablement of the composition disclosed therein- the IC41 composition comprising the declaration peptides and the poly-L-arginine adjuvant. However, when making a determination as to whether evidence provided by the Applicant enables a claimed invention, one of the concerns to be considered is "whether the scope of

enablement provided to one skilled in the art by the disclosure is commensurate with the scope of protection sought by the claims." See e.g., *AK Steel Corp. v. Sollac*, 68 USPQ2d 1280, 1287 (Fed. Cir. 2003); and MPEP 2164.08. In the present case, the enabling disclosure is not commensurate in scope with the protection being sought.

The claims under consideration are not drawn to the specific composition (IC41) described in the declaration. Rather, they are drawn broadly to compositions comprising an epitope found within each of the three peptides of claim 34. In fact, it is noted that elected invention (compositions comprising the three peptides of amended claim 34), is not drawn to the IC41 vaccine. Rather, the claims and the elected composition generally require only three of the five peptides of the IC41 vaccine, and are claimed in absence of the poly-L-arginine adjuvant used in the IC41 vaccine. However, neither the data of the application or the Wedemeyer declaration provide any indication as to which of the peptides included in the vaccine are necessary. I.e., neither the declaration nor the application provides teachings regarding the correlates of efficacy for the disclosed vaccine. As was indicated in the prior action, such teachings are also absent from the art. In fact, one of the grounds of uncertainty in the art of HCV vaccines is the lack of knowledge regarding the correlates of protection against the virus. Because these correlates of protection were not known in the art, and are not disclosed by the application or the declaration, it is not clear that any composition comprising any one or more, but not all, of the peptides of IC41 would alone be sufficient to achieve a therapeutic effect.

Further, claim 34 does not even require the full length of the peptides, but merely requires that "an epitope" of such peptides is present. It is noted that at least the peptide of SEQ ID NO: 63 includes multiple epitopes. See e.g., Wentworth et al., Int Immunol 8:651-59, at 654

(Table 4, peptides NS4 1769 and NS4 1773- reference of record in the April 2007 IDS). Again, absent knowledge in the art of the correlates of protection, it is not clear that any peptide comprising less than all of the epitopes found in the peptides of IC41 would be capable of inducing the required therapeutic response.

Thus, the teachings of even the Wedemeyer declaration are insufficient to demonstrate enablement for the full scope of the invention as claimed.

In view of the uncertainty, complexity, and limited understanding in the art, the limited evidence of therapeutic efficacy provided by the application, and the fact that the rejected claims are not limited to the embodiment described by the Wedemeyer, declaration, the rejection is maintained.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. **(Prior Rejection- Withdrawn)** Claims 34, 35, 39, and 40 were rejected under 35 U.S.C. 103(a) as being unpatentable over Wentworth et al. (Int Immunol 8:651-59- of record in the April 2007 IDS). In view of the amendment of the claims to require the presence of epitopes from each of SEQ ID NOs: 17, 60, and 63; and as epitopes from each of these sequences have not been disclosed by the rejection, the rejection is withdrawn.

11. **(Prior Rejection- Maintained)** Claims 34. 35, 39, 40, 48, 60, 62, and 64 were rejected under 35 U.S.C. 103(a) as being unpatentable over Diepolder et al. (J Virol 71: 6011-19), Cerny et al. (J Clin Invest 95: 521-30), and Lamonaca et al. (Hepatology 30:1088-98). The rejection is withdrawn from cancelled claims 35, 62, and 64; but is maintained against pending claims 34, 39, 40, 48, and 60.

The Applicant traverses the rejection on three grounds.

First, the Applicant asserts that there would not have been adequate motivation for those of ordinary skill in the art to combine the peptides of these references to arrive at the claimed composition. The Applicant provides no support for this assertion. Moreover, motivation for the combination was provides in the prior action. This argument is therefore not found persuasive.

Each of the second and third arguments is based on secondary evidence of non-obviousness. The Applicant asserts that the claimed invention meets a long-felt and unresolved need in the art, and achieves unexpected results over what would have been expected from the teachings of the prior art. Neither of these arguments is found persuasive for the reasons described above with respect to the scope of the teachings of the Wedemeyer declaration. I.e., the present claims are not commensurate in scope with the evidence of therapeutic efficacy provided by the Applicant (which efficacy represents both the long-felt need and the unexpected results asserted by the Applicant). Because the claims are not commensurate in scope with the evidence relied on to support the secondary basis for finding non-obviousness, these arguments relying on the unexpected results and the satisfaction of the long-felt need are not found persuasive. The rejection is therefore maintained.

12. **(Prior Rejection- Maintained)** Claims 39, 48, 61, 64, and 65 were rejected under 35 U.S.C. 103(a) as being unpatentable over Diepolder, Cerny, and Lamonaca as applied above, and further in view of Wentworth (supra), Day et al. (J Virol 76:12584-595), and Alexander (Human Immunol 59:776-82), and of Van Der Berg (WO 02/70006), Abrams et al. (Cell Immunol 182:137-51), and Chisari et al. (U.S. 2002/0115061). This rejection is withdrawn from cancelled claims 61, 64, and 65, but is maintained over claims 39 and 48. The Applicant traverses the rejection on the same grounds as asserted above with respect to the rejection of claims 34, 39, 40, 48, and 60 over the teachings of Diepolder, Cerny, and Lamonaca, These arguments are not found persuasive for the reasons indicated above. The rejection is therefore maintained for the reasons above and the reasons of record.

13. **(Prior Rejection- Maintained in part)** Claims 72 and 73 were rejected under 35 U.S.C. 103(a) as being unpatentable over either of Wentworth as applied to claims 34, 35, 39, and 40 above; or of Diepolder, Cerny, and Lamonaca as applied to claims 34. 35, 39, 40, 48, 60, 62, and 64 above, further in view of Schmidt et al. (WO 01/93905). The rejection is maintained to the extent that it relies on the teachings of Diepolder, Cerny, and Lamonaca in view of Schmidt. The Applicant traverses the rejection on the same grounds as asserted above with respect to the rejection of claims 34, 39, 40, 48, and 60 over the teachings of Diepolder, Cerny, and Lamonaca, These arguments are not found persuasive for the reasons indicated above. The rejection is therefore maintained for the reasons above and the reasons of record.

14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Double Patenting

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. **(Prior Rejection- Maintained)** Claims 34, 35, 36, 4048, 60-62, 64, and 65 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16-24 of copending Application No. 11/082595 No argument in

traversal has been made with respect to the present rejection. The rejection is therefore maintained.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

It is noted that the copending application has an earlier priority date than the present application. As such, and contrary to the assertion by the Applicant, this rejection will not be withdrawn even if it is the only remaining rejection in the present application as per MPEP 804 I.B.1 so long as the copending earlier application still has pending claims over which the rejection may be maintained.

Conclusion

17. No claims are allowed.

18. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is (571)272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Zachariah Lucas/
Primary Examiner, Art Unit 1648